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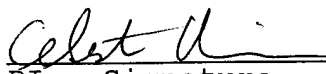
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INTRODUCTION

It is estimated that nearly one in nine women in the United States will develop breast cancer at some point in their lives [1]. Early detection will greatly improve a woman's chance of survival. Presently, the imaging techniques used for diagnosis and detection of breast cancer are all performed by deforming the breast from its original shape. The shape deformation employed by such imaging techniques present improved diagnostic imaging of the breast, however, the imaging techniques do not take into account the biomechanical nature of breast tissue. This is largely due to the fact that the biomechanical behavior of breast tissue is not fully understood. If the normal and pathological mechanical behavior of soft tissue can be better understood, it may be possible to identify pathologies. Most importantly, the understanding of the biomechanical properties of breast tissue may be used to develop more accurate breast models. Such biomechanically-based models can be used to develop computer morphing algorithms so that the initial images obtained by shape deformation can be transformed into images that represent the breast in an undeformed state. Such images will better aid in surgical biopsies and breast conservation procedures, and may improve the prognosis for breast cancer patients.

The primary purpose of our study is to investigate the biomechanical nature of normal breast tissue undergoing shape deformation due to external forces that are routinely used in diagnostic imaging of breast disease. This report describes the preliminary study of the first task of the BAA proposal.

Background

Task One involved the identification of MR-visible internal and external landmarks. In order to improve shape modeling, and interpret shape deformation. MR-visible landmarks are identified in both the human breast and breast phantoms. Biological landmarks are characterized as points that have biological names, such as rib cage or nipple, as well as geometric locations [2]. Landmarks help to link the mathematics of deformation and the forces which act on the landmarks. The three principle types of landmarks applied in our study are:

- 1). Juxtapositions of tissues, points in space at which two or more structures meet
- 2). Maxima or Minima of curvature, such as tips of extrusions and valleys of vaginations
- 3). Extremal or tangential points

Several studies have investigated techniques of computer analysis of images using external landmarks. Such techniques are utilized in 3D image reconstruction for the design of craniofacial surgical procedures, and for vascular imaging [3,4,5].

BODY OF REPORT

Methods

MRI

Preliminary studies were conducted on both phantoms and healthy female subjects. All breast models were imaged with MRI. Various magnetic resonance imaging techniques were used to identify promising internal landmarks and to characterize external landmarks. All images were acquired on a 1.5 T clinical MRI system (General Electric, Signa).

BREAST MODELS

Types of Phantoms

Breast Prosthesis: This a mold of silicon in the shape of a human breast that is routinely used for external breast augmentation. The breast prosthesis is affixed to a plaster cast of a chest wall to simulate the curvature of the chest.

Silicon-Saline Implants: These implants are round, 15 cm, gel-filled mammary prostheses, that are routinely used for tissue replacement following mastectomies. The prostheses possess two chambers, an inner silicon-filled envelope, and an outer envelope that is filled with normal saline. The outer envelope has low modular properties and the elasticity can be varied by changing the volume of saline in this chamber.

Human Subjects

Existing data from several healthy female volunteers, over the age of 18, were identified. The subjects were all pre-menopausal women, and written informed consent was obtained according to a currently active MRI protocol approved by the Ohio State University Biomedical Sciences Human Subjects Review Committee.

Results and Discussion

EXTERNAL LANDMARK STUDIES

Identification of External Landmarks

External MR-visible markers were placed in a grid or mesh pattern on the surface of the phantom. Various materials, which could be safely placed in an MRI system, were tested to ascertain their suitability as positional markers. Among the materials tested were vitamin-E capsules, lip balm, GAK, water-based paints, paints with metallic content, and metallic stickers.

These materials were placed on a gelatin surface and imaged with T1- and T2-weighted spin echo and gradient echo MR imaging sequences.

Materials, such as the capsules and the lip balm, contain a large oil content that increase the signal intensity on MR images, so that such materials appeared very bright. The materials with the metallic content caused susceptibility effects on the MR images and generated small local signal voids. Initial tests indicated that the nail-polish containing metallic material was the most suitable external marker, both in terms of marking out grid points and for the size of local changes.

How External Markers Affect MR Signal

In the phantom tests using the prosthesis breast model, the model was marked with both the vitamin-E capsules and the metallic polish. The oval-shaped vitamin capsules were taped, in a grid pattern, to the elastic surface enveloping the prosthesis. The metallic polish was placed in a grid pattern, with lattice points about 1 inch apart, on both the inner (chest wall) and outer sides of the prosthesis. The model was imaged in the supine position with a T1-weighted spin echo sequence. This supine imaging provided initial testing of deformation algorithms. The image is shown in Figure 1. As can be seen, the surface material covering the prosthesis does not sufficiently deform from the supine to prone position. The vitamin-E markers provide a large signal-to-noise ratio, and are good identifiable landmarks. However, the size of the capsules, (3mm), makes for a bulky grid. With the metallic polish, the voids due to signal aliasing prove to be a problem because the signal starts to overlap, creating voids that are much larger than the lattice points of metallic polish. This problem can be solved by smaller spots of polish making the grid lattice points wider than 1 inch apart.

INTERNAL LANDMARK STUDIES

In the human breast studies, anatomical features such as the rib cage, branching ducts, fatty tissue, boundaries between glandular and fatty tissue and the nipple were used to define landmarks. These features are clearly visible on the MR images shown in Figure 2. MR images of healthy subjects were acquired using a commercial phased array breast coil. Internal landmarks of the human breast were identified from these initial MR images of the subjects lying prone with the breast hanging freely in the breast coil. Different image contrast and resolution imaging were tested. The various imaging sequences used are given in Table 1. All sequences had image acquisition times between 3-6 minutes.

TABLE 1. MR Imaging Sequences.

Sequence #	1	2	3	4	5
Plane	axial	sagittal	sagittal	sagittal	sagittal
Sequence	T1-weighted 2D spin echo	T2-weighted 2D fast spin echo	2D gradient echo	2D gradient echo	T1 weighted 3D spoiled gradient echo
TR	700 ms	7000 ms	11.2 ms	11.2 ms	19 ms
TE	10 ms	100 ms	2.9 ms	4.2 ms	4.2 ms
flip/ETL		16 ETL	25 degrees	25 degrees	25 degrees
resolution	0.4x0.4 mm	0.8x0.8 mm	0.8x1.8mm	0,8x1.6mm	0.4x0.4mm
slice thickness	5 mm	5 mm	5 mm	5 mm	2 mm
signal avg.	1	1	4	4	1

With sequence number 3, images were acquired with low resolution and with TE's of 2.9ms and 4.2ms. For TE of 2.9ms, fat and water magnetization are out-of-phase and thus all image volume elements that contain fat and water give a reduced signal, leading to dark outlines between the boundaries of fatty and glandular tissue. For TE of 4.2 ms, fat and water magnetization are in-phase and the signal from fat and water components add up and the boundary voxels have intermediate signal. The purpose of this comparison was to evaluate if the dark tissue boundary outlines could provide useful landmarks. However, with the low slice resolution, this was not useful because relatively broad dark bands were observed due to signal combination across the thick slices. Further tests with higher resolution are needed to assess the usefulness of this boundary approach.

Optimal Imaging Protocol

High resolution images were acquired with sequence number 5. These initial tests indicate that image characteristics suitable for landmark identification may best be obtained with T1-weighted high resolution imaging. The high resolution image is shown in Figure 2. The adipose tissue appears brighter with a high SNR. Glandular tissue has low signal and appears darker. One volunteer was studied with this optimal high resolution protocol in the prone position using the breast coil and in supine position using a body coil. The two images are shown in Figure 3. The MR image is a 3D sagittal image of the right breast. The supine image has a low SNR and appears noisy because of motion artifacts due to cardiac and respiratory motion.

Figure 2 and figure 3 were obtained from two different subjects and the images are clearly distinguishable, each displaying unique landmarks. The subject in figure 2 has more glandular tissue which is more symmetrical in shape. The subject in figure 3 has less glandular tissue and more adipose. Also the glandular tissue has a less symmetrical and more spiculated appearance. The difference in age between the two young subjects is about 4 years.

The number 1 indicates the nipple landmark. The number 2 indicates the rib cage. Number 3 indicates type one landmarks that are points in space at which two or more structures meet. Number 4 indicates type two landmarks that are tips of extrusions and valleys. The corresponding landmarks are found in both the prone and supine images. A computer morphing algorithm will be developed which maps such landmarks from the source (prone image) to the target (supine image).

BREATH-HOLD IMAGING

In order to reduce the motion artifacts, several acquisition protocols were explored using breath-hold imaging. Breath-hold imaging requires sequences that permit image acquisition in less than 30 seconds. We tested a 3D fast gradient echo sequence. Twelve slices with $0.31 \times 2.5 \times 2.0$ mm voxel size were acquired simultaneously for both breasts. The SNR in these images was poor. Images were also obtained with a T1-weighted fast spin echo sequence using TE of 500 ms, TE of 17ms, echo train length of 4, and a voxel size of $1.2 \times 11.7 \times 5.0$ mm. While the FSE (fast spin echo) approach appeared to be more promising, further studies are needed to improve SNR and image quality.

Several new fast imaging techniques will become available after installation of fast gradient hardware at the end of this month. This includes a fast 3D gradient echo sequences, improved fast spin echo sequences, and echo planar imaging sequences. With these techniques, it will be possible to either increase the spatial resolution or to speed-up image acquisition, or both. A series of studies will be carried out to evaluate these new methods for high quality breath-hold breast imaging. We will also attempt to improve image quality of supine imaging by using various surface coils.

INITIAL MORPHING ALGORITHMS

Using the initial high-resolution MR images, internal landmark data, shown in Figure 4, were selected for use in the preliminary studies of morphing algorithms. Free-form deformation (FFD) is a 2D morphing technique using the spline interpolation approach in which a grid lattice cage envelopes the object of deformation, see figure 5. In this method the object is not deformed directly, but it is embedded in a space which is deformed instead. As the points (or vertices) of the lattice move, the object deforms according to the shape of its metal cage. This approach is simple but it does not take in to account the overlapping or intersection of lattice points as they move.

Another approach under investigation is 3D volume morphing, shown in figure 6. In this method, points of the simple model are fixed and other points are selected for movement, such as rotation or compression. As the points move, the volume follows and the intersection of points is not a problem. This algorithm is only in its initial stage and because of computation time, only small image sizes are possible.

CONCLUSION

Materials with high metallic content are promising as external MR-visible markers. They are easily applied to the surface of breast models and they provide a distinguishable MR signal. The anatomical structures of the breast are reliable internal landmarks. Both types of landmarks allow localization of tissue deformation and definition of coordinates of lesions. Using a high resolution MR imaging technique, high quality prone images can be acquired in under six minutes. It is possible to conceal the motion artifacts of supine imaging through the use of fast imaging breath-hold techniques. Such breath-hold techniques will permit acquisition of high quality supine images in about 30 seconds.

With the 3D volumetric data, generated by MR imaging, the deformation of breast tissue is readily obtained by comparing the voxel locations between landmarks of the un-deformed image to the voxel locations in the deformed image. With this deformation data, accurate breast models, based on the biomechanical nature of breast tissue, may be developed.

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APPENDICES

a. Acronyms and Symbols

T - tesla

TR - repetition time

TE - echo time

T1- spin-lattice relaxation time of the magnetization along the longitudinal axis

T2- spin-spin relaxation time of magnetization in the transverse plane.

ETL - echo train length

ms - millisecond

mm - millimeter

SNR - signal-to-noise ratio

FSE - fast spin echo

2D - two dimensional

3D - three dimensional

b. FIGURES

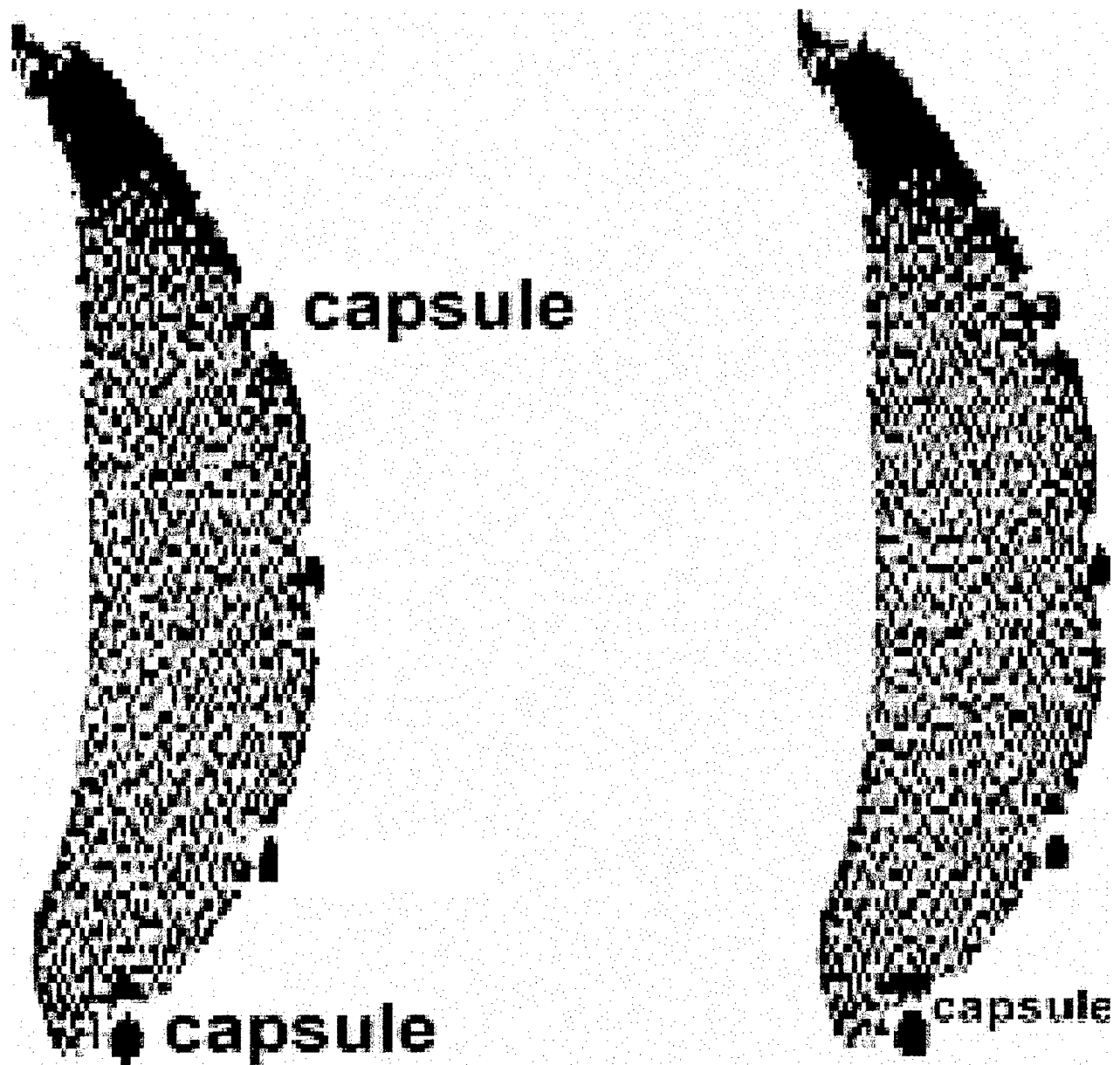
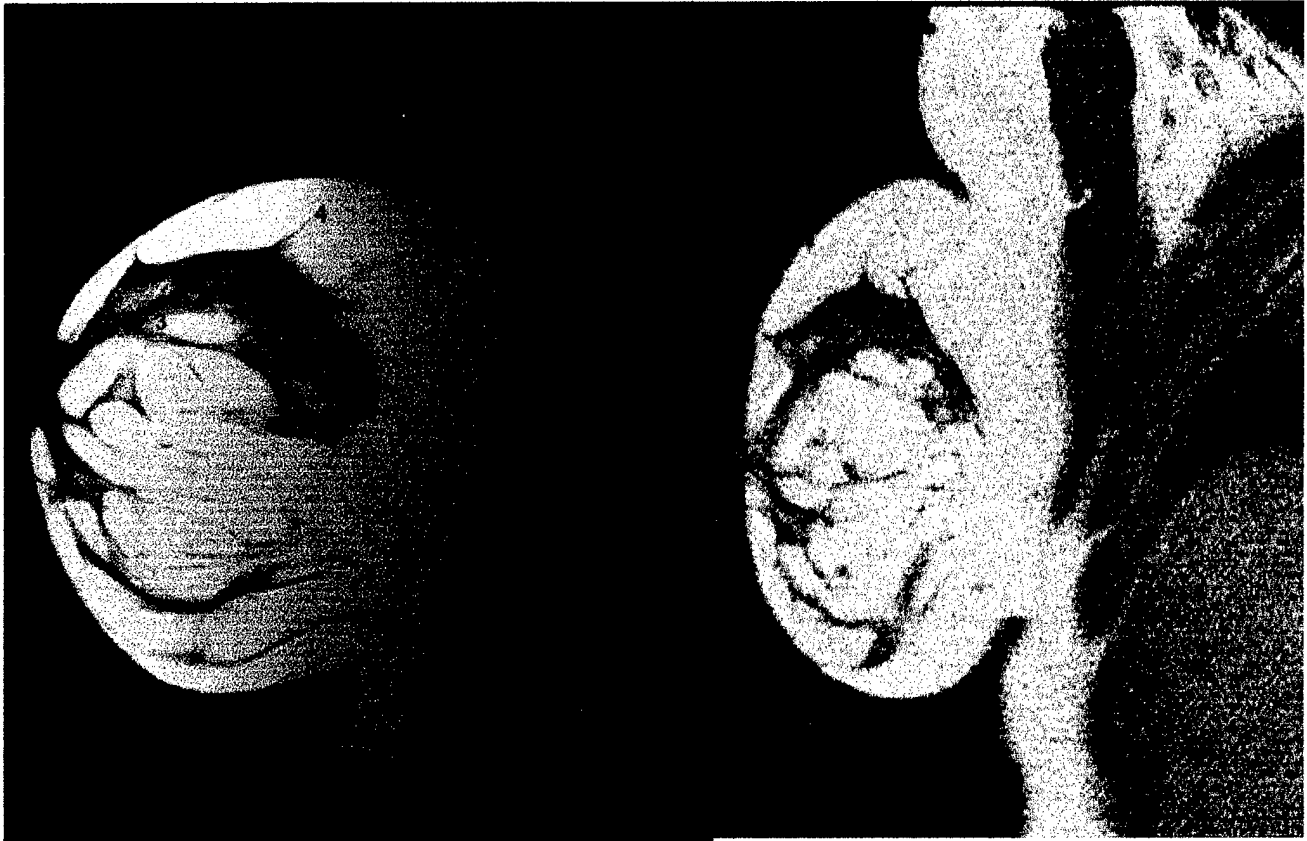


Figure 1. Prosthesis with external landmarks.



Figure 2. Internal landmarks of subject 1.
High resolution prone image



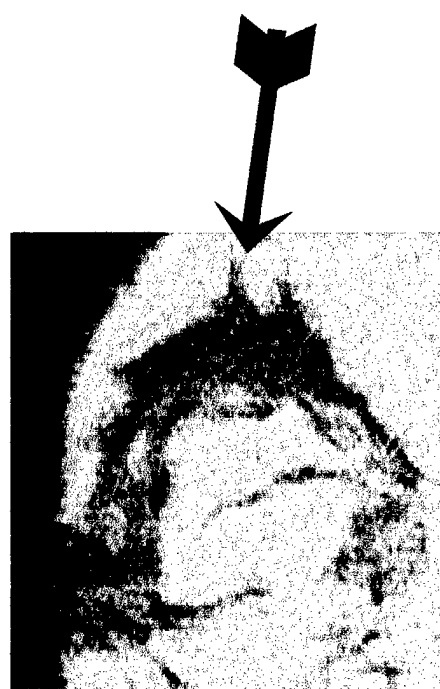
(a) prone

(b) supine

Figure 3. High resolution images of subject 2.
a) prone, b) supine



(a) prone



(b) supine

Figure 4. Morphing landmark data taken from HR images.

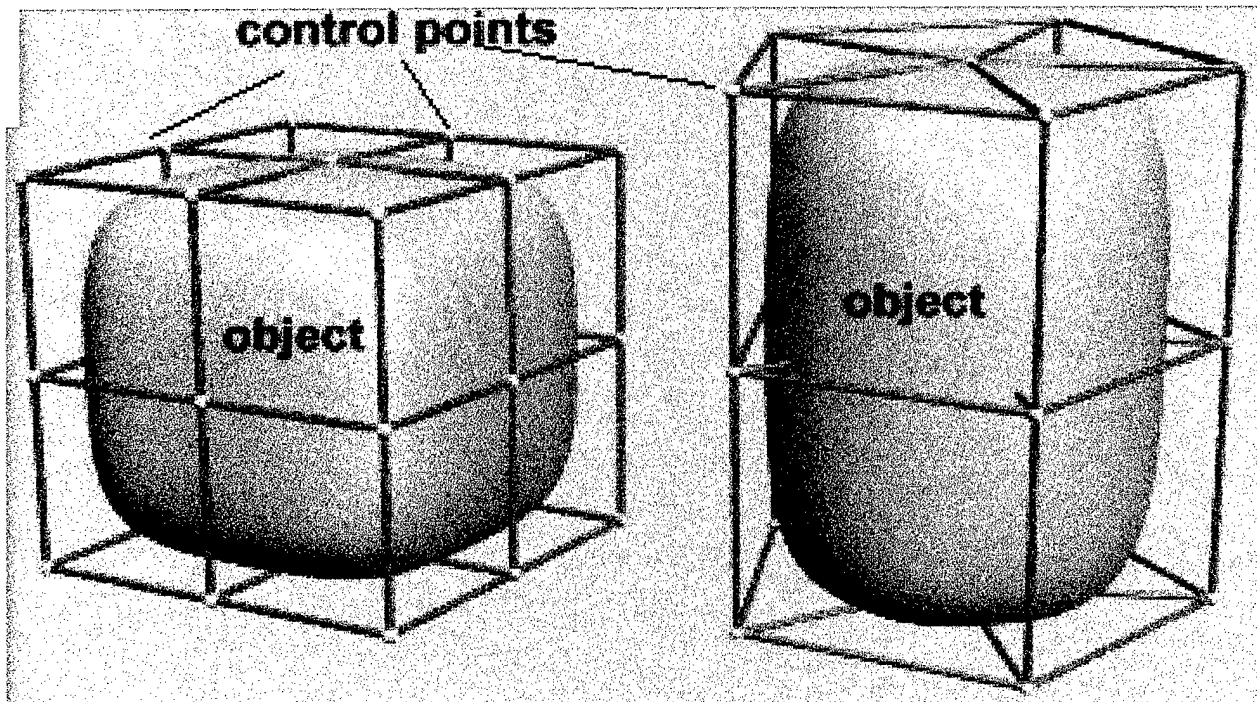


Figure 5. FFD (free form deformation) morphing algorithm. Control points deform the lattice grid.

c. MRI Biomedical Sciences Review Committee

BIOMEDICAL SCIENCES REVIEW COMMITTEE
RESEARCH INVOLVING HUMAN SUBJECTS
THE OHIO STATE UNIVERSITY

☐ Original Review
☒ Continuing Review
☐ Five-Year Review
☐ Amendment

ACTION OF THE REVIEW COMMITTEE

With regard to the employment of human subjects in the proposed research:

91H0301 SUBMILLIMETER RESOLUTION IMAGING USING A MAGNETIC RESONANCE
DEVICE, Petra Schmalbrock, Radiology

☒ APPROVED

☐ DISAPPROVED

☐ APPROVED WITH STIPULATIONS*

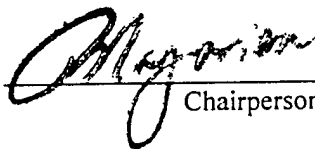
☐ WAIVER OF WRITTEN
CONSENT GRANTED

*Stipulations stated by the Committee have been met by the investigator and, therefore, the protocol is
APPROVED>

It is the responsibility of the principal investigator to retain a copy of **each** signed consent form for at least three (3) years beyond the termination of the subject's participation in the proposed activity. Should the principal investigator leave the University, signed consent forms are to be transferred to the Human Subjects Committee for the required retention period. This application has been approved for the period of one year. You are reminded that you must promptly report any problems to the Review Committee, and that no procedural changes may be made without prior review and approval. You are also reminded that the identity of the research participants must be kept confidential.

Date: May 20, 1996

Signed



Chairperson

HS-025H (Rev. 2/94)

CONSENT TO INVESTIGATIONAL TREATMENT OR PROCEDURE

I, _____, hereby authorize or direct Petra Schmalbrock, Ph.D., her associates or assistants of her choosing, to perform the following treatment or procedure (described in general terms).

to obtain experimental diagnostic pictures of my body by using a Magnetic Resonance Diagnostic Device, which uses magnets and radio waves. No cost will occur for the exam.

The experimental (research) portion of the treatment or procedure is:

The use of modified computer programs to control the operation of the device (previously tested on phantoms) and/or specialized radio frequency coils.

This is done as part of an investigation entitled:

Sub-millimeter Resolution Imaging Using a Magnetic Resonance Device.

1. Purpose of the procedure or treatment:

The purpose of the research is to test new methods and to assess the diagnostic reliability of Magnetic Resonance for the generation of images that show very small (less than 1 mm) anatomic structures.

2. Possible appropriate alternative procedures or treatment (not to participate in the study is always an option):

Not to participate. The device is not intended to deliver treatment, but is used only as a diagnostic tool. No diagnosis will be based on the experimental MR data alone.

3. Discomforts and risks reasonable to be expected:

a) I may experience transient feelings of being closed in (claustrophobia).

b) A soft hammering noise will be heard as the device steps through electronic switches.

c) To synchronize the data acquisition with the heart rate, EKG lead cables may be connected to my skin with adhesive patches. This may cause minor skin irritation and discomfort.

d) No medical risks are known. Because this is experimental, there may be unknown risks. Induced electric currents or movement of metallic objects can occur. Patient with known contraindication of MRI will be excluded. Long-term effects of MR are not known at this time.

4. Possible benefits for subjects/society:

MR may provide a safe way to obtain information of anatomic details with high resolution. To compensate for the inconvenience, participants in late night studies will be paid \$20.

5. Anticipated duration of subject's participation (including number of visits):

Typically less than 2 hours.

I hereby acknowledged that _____ has provided information about the procedure described above, about my rights as a subject, and he/she answered all questions to my satisfaction. I understand that I may contact him/her at phone No. 293/5172 should I have additional questions. He/she has explained the risks described above and I understand them; he/she has offered to explain all possible risks or complications. I understand that, where appropriate, the U.S. Food and Drug Administration may inspect records pertaining to this study. I understand further that records obtained during my participation in this study that may contain my name or other personal identifiers may be made available to the sponsor of this study. Beyond this, I understand that my participation will remain confidential.

I understand that I am free to withdraw my consent and participation in this project at any time after notifying the project director without prejudicing future care. No guarantee has been given to me concerning this treatment or procedure.

I understand that in signing this form that, beyond giving consent, I am not waiving any legal rights that I might otherwise have, and I am not releasing the investigator, the sponsor, the institution, or its agents from any legal liability for damages that they might otherwise have.

In the unlikely event of injury resulting from participation in this study, I understand that immediate medical treatment is available at University Hospital of The Ohio State University. I also understand that the cost of such treatment will be at my expense and that financial compensation is not available. Questions about this should be directed to the Human Subjects Review Office at 292-9046.

I have read and fully understand the consent form. I sign it freely and voluntarily. A copy has been given to me.

Date: _____ Time _____ AM/PM Signed _____

(Subject)

Witness(es) _____

if _____ (Person Authorized to Consent
Required _____ for Subject, if Required)

I certify that I have personally completed all blanks in this form and explained them to the subject or his/her representative before requesting the subject or his/her representative to sign it.

Signed _____

(Signature of Project Director or his/her Authorized Representative)